(12) (19) (CA) **Brevet-Patent**



(11)(21)(C) **2,095,439**

(86) 1991/12/05

(87) 1992/06/07 (45) 1998/12/08

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(51) Int.Cl.⁶ A61K 31/375, A61K 9/20, A61K 9/14, A61K 9/08

(30) 1990/12/06 (07/624,094) US

(54) SUBSTANCE ARRETANT LE SAIGNEMENT AU CONTACT POUR USAGE MEDICAL, CHIRURGICAL ET DENTAIRE

(54) SUBSTANCE THAT STOPS ANY BLEEDING ON CONTACT FOR MEDICAL, SURGICAL AND DENTAL USES

(57) Divulgation d'une méthode pour arrêter le saignement et former un caillot noir de sang au contact, consistant à administrer de la L-thréo-hex-2-énono-1,4lactone en poudre sur la plaie dans un rapport de 0,1568 gramme par millilitre de sang. La substance arrête les hémorragies reliées au cancer, à la maladie du foie et à l'hémophilie chez les patients ou les animaux atteints de troubles liés à la thrombocytopénie ou aux facteurs de coagulation. De la même façon, le mécanisme d'action de la L-thréo-hex-2-énono-1,4-lactone en poudre qui fait coaguler le sang au contact est l'unique voie extrinsèque commune d'activation de la coagulation du sang, qui rejette les mécanismes des voies intrinsèque et extrinsèque de la cascade de coagulation du sang comme étant les seules voies d'activation de la coagulation du sang nécessitant l'intervention des facteurs de coagulation 1, 2, 5, 7, 8, 9, 10 et le facteur 3 des plaquettes.

(57) There is disclosed a method for stopping bleeding and forming black blood coagulation on contact, comprising administering powdered L-threo-hex-2enono-1,4-lactone thereof to a wound site in an amount of 0.1568 grams for every milliliter of blood. This includes cancer, liver disease and hemophiliac bleeding in patients or animals in whom the thrombocytopenia or coagulation factor disorders result. Accordingly, the said mechanism of action of powdered L-threo-hex-2-enono-1,4-lactone in the formation of blood coagulation on contact is the unique common pathway for all blood coagulations, which overturns the mechanisms of intrinsic and extrinsic pathways for blood coagulation cascade being the unique pathways for blood coagulation in which the coagulation factors 1, 2, 5, 7, 8, 9, 10 and platelet factor 3 are essential for the pathways.

ABSTRACT

There is disclosed a method for stopping bleeding and forming black blood coagulation on contact, comprising administering powdered L-threo-hex-2-enono-1,4-lactone thereof to a wound site in an amount of 0.1568 grams for every milliliter of blood. This includes cancer, liver disease and hemophiliac bleeding in patients or animals in whom the thrombocytopenia or coagulation factor disorders result. Accordingly, the said mechanism of action of powdered L-threo-hex-2-enono-1,4-lactone in the formation of blood coagulation on contact is the unique common pathway for all blood coagulations, which overturns the mechanisms of intrinsic and extrinsic pathways for blood coagulation cascade being the unique pathways for blood coagulation in which the coagulation factors 1, 2, 5, 7, 8, 9, 10 and platelet factor 3 are essential for the pathways.

SUBSTITUTE SPECIFICATION

CROSS REFERENCE RELATED TO APPLICATION

This application is an international application for U.S. application Serial No. 07/624,094, filed 06 December, 1990.

BACKGROUND OF THE INVENTION

The present invention pertains to the field of blood coagulation, which is further related to evaluation of coagulation tests ; e. g. prothrombin time, partial thromboplastin time and activated partial thromboplastin time etc, and coaqulation factor disorders. However, the blood coaqulation mechanism of action of powdered L-Ascorbic acid which was administered topically does not fall into either intrinsic or extrinsic pathway cascade of blood coagulation scheme, since it works the same for blood coagulation in normal situation as in chronic hepatitis, colon cancer, and hemophilia patients in whom the coagulation factors 1, 2, 5, 7, 9, and 10 and platelets in the liver disease and factor 8 or 9 in the hemophilia A or B are abnormal, or suppressed the syntheses, and destroyed and deficient (Harrison's Principles of Internal Medicine, 12th Edition, 1991, Pages 1314-1315). In other words, powdered L-Ascorbic acid or L-threo-hex-2-enono-1,4-lactone stops any bleeding and forms black blood coagulation on contact, with the same amount of powdered L-Ascorbic acid per unit volume of blood for any normal or diseased blood.

The present methods available to stop bleeding in surgery are cautery, epinephrine injection, pressure and some fiber foam. The cautery can cause tissue necrosis in some cases. The epinephrine, pressure and fiber foam can not work for bleeding tendency patients, and fiber foam can cause tissue hematoma, nor can they work for diffuse capillary bleeding and oozing, while powdered ascorbic acid does not cause any tissue necrosis and work particularly well for diffuse capillary bleeding and oozing and any traditionary uncontrollable bleeding tendency patients such as for patients with liver diseases, hemophilia and rectal anal cancer and for postoperation bleeding tendency of the kinds of aforementioned patients. The ascorbic acid can facilitate wound healing also (Ora-1 Surg 1982 Mar: 53(3): 231-6) by increasing type 1 procollagen

 \rightarrow nRNA in the regulation of collagen synthesis (Atherosclerosis 1982 Jan: 41(1): 15-9).

SUMMARY OF THE INVENTION

The present invention is directed to a method for stopping bleeding, comprising administering powdered vitamin C thereof to the wound site caused by pathological changes, trauma or surgery, in an amount of 0.1568 grams for every milliliter of blood. Powdered L-threo-hex-2-enono-1,4-lactone represents ascorbic acid powder. This powder has a very potent coagulation action to stop bleeding when spraying topically on the bleeding area for any normal or diseased patients. When the powder comes in contact with the blood, the black tar like material is formed, and later becomes solid. The amount of the powder that is needed to react completely with the blood is proportional to the amount of the blood that comes out of the blood vessels. In rats, one capillary, one venous and one femoral artery bleeding were stanched within one second, if sufficient amount of the powder of ascorbic acid were applied. The artery bleeding needs much more this powder of interest. In the test tube conditions, it requires 0.1568 grams of powdered L-Ascorbic acid or L-threo-hex-2-enono-1,4-lactone added to 1 ml of any normal or diseased human blood to turn the mixture black and, after 6 minutes, it does not move by shaking or pouring; this is the same for normal, colon cancer and hemophilia patients; 1 ml of normal blood needs 0,1568 grams of ascorbic acid powder, 1 ml of colon cancer needs 0.1568 grams of ascorbic acid powder, and 1 ml of hemophilia blood needs 0.1568 grams of ascorbic acid powder. Sufficient powdered L-threo-hex-2-enono-1,4-lactone is particularly useful to stop bleeding in the case of diffuse capillary oozing and mistakenly cut off artery or arteries that can not be found during massive bleeding so as to save the patients's lives therefor. When vitamin C is absorbed into the system, it is good for health by making the leucocytes stronger and slowing the aging process etc, (Patnaik and Kanungo 1964, Gerontologia, 10, 155). However, at the end of operation before closure, the excessive black tar gel like material can be wiped away with Ringer's solution.

DETAILED DESCRIPTION OF THE INVENTION

The present invention is grounded on applicant's discovery that any bleeding, either normal or diseased blood, is stopped on contact, and is formed black blood coagulation, by administration topically of a composition comprising powdered vitamin C to the bleeding sites even when contaminated with impurities, and excipients, in an amount of 0.1568 grams of powdered vitamin C for every milliliter of blood. A composition comprising powdered vitamin C is made by making vitamin C tablets into powder. A vitamin C tablets, of course, contains impurities, and excipients other than vitamin C. While the present method is particularly directed at treatment of bleeding in humans it finds the same application for veterinary use. As the liver is the site of syntheses of all coagulation factors except 8, prior to the present invention, nothing has, to the best of my knowledge, been made to stop bleeding on contact, for the massive bleeding tendency patients afflicated with liver diseases, cancer or hemophilia. The treatment for hepatic coagulopathy and hemophilia is the replacement therapy for transfusion of fresh frozen plasma and factor 8 or 9 concentrates respectively, Lawrence M. Tierney, Jr., et al, Current Medical Diagnosis & Treatment, 1994, 33rd Annual Revision, 458-459, but that will not bleeding on time in a wound caused by trauma or surgery; some patients bled to death simply because of extraction of teeth or tonsilectomy. As soon as a composition comprising powdered vitamin C contacts with b1ood, even in massive bleeding when an artery of a rat is cut off, the black gel film like structure forms on the surface of the pond of blood, that stops the fluid of blood moving. If stirring the blood to break through the surface film like structure that keeps fluid from moving when the powder is insufficient, it will bleed again, but much slower than before pouring into the bleeding area; adding sufficient powder into the blood, stirring makes the powder molecules well saturated with the hemoglobin and plasma protein mocules and thus forming the concentrated black sticky gel like structure.

The invention is further illustrated in the following examples, none of which are to be construed as limiting the invention in any respect. The following example reports the results of an animal study and a clinical evidence of a composition or the present invention in the treatment of bleeding.

ANIMAL EXPERIMENTS EXAMPLE 1

Sufficient composition comprising powdered vitamin C stops massive bleeding of femoral artery on contact when femoral artery of a rat is cut off. In this case of artery bleeding, it is administered topically by pouring instead of spraying. Although the amount of the powder needed varies with rats, 0.1344 grams is usually sufficient to stop bleeding within one second for the femoral artery of a rat. The black tar like material is formed in one second as soon as the powder contacts with the blood. When sufficient amount of powdered vitamin C is present, stirring make more blood molecules interact with ascorbic acid molecules so as to form more concentrated and sticky black gel like coagulation. After 5-6 minutes, when most of the sticky tar like structure is wiped away, it appears there is no bleeding at all.

EXAMPLE 2

In the case of capillary bleeding in which one capillary is cut off, about 0.0112 grams of this powder stops the bleeding on contact. After 1 minute count from adding the powder, it appears there is no more bleeding at all in a rat.

EXAMPLE 3

While in the case of one vein cut off in a rat, it needs about 0. 0224 grams of the powder to stop bleeding on contact, about 1 1/2 minutes after the black coagulation is wiped away, it appears there is no more bleeding.

EXAMPLE 4

The nostril of a rat is cut slightly to bleed, the bleeding stops on contact when applying 0.0037 grams of this powder to the bleeding nostril.

EXAMPLE 5

After injection of histamin into the rat, it induces secretion of gastric acid, applying the powder topically to the bleeding area, the black coagulation formed, but slower than normal, since the secretion dilutes the black coagulation. Thus this powder can treat the gastric ulcer bleeding when ingested orally.

CLINICAL EVIDENCE EXAMPLE 6

Scalp Tumor Excision

Age 32, male, scalp tumor excision, massive bleeding when the tumor is excised. Sufficient spraying this powder to the bleeding area, the bleeding stops on contact, after the coagulation is washed away, it is closed by suture.

EXAMPLE 7

A-V Fistula Plasty

Age 40, female, acute renal failure, A-V fistula formation operation, massive bleeding. The operation of stopping bleeding consists of combing the powder with pressing with gauzes. When administering this powder to the bleeding area, those that look black in color indicate the black coagulation, while those that are white are the powder that does not get mixed up with the blood yet. At the end of the operation, most of black blood coagulation is wiped out with 4x4 gauze, and rinsed with Ringer's solution. It takes totally 5 minutes to stop bleeding completely, as the surgeon kept wiping away the coagulation. The patient's conditions are particularly well, better than without using this powder.

EXAMPLE 8

Skin Contracture Excision

Age 40, male, skin contracture on the palm, which needs to be removed, and it requires skin graft. When the skin graft is removed from the hand, massive bleeding occurs. On applying sufficient powder to the bleeding area topically, it appears black coagulation on contact. Bleeding stops at the same time as the black coagulation forms. Those that appears white indicate the powder not yet get mixed up with the blood. Those that appears more black area indicate the more powder mixed up with the blood. Suture going on.

EXAMPLE 9

Paraanal Abscess Excision

Age 70, female, paraanal excision, bleeding when it is opened up. When spraying the powder to the bleeding area, it stops bleeding by forming black blood coagulation on contact. Those that appears white are the powder that are not mixed up with the blood. Suture going on.

EXAMPLE 10

Paraanal Abscess Excision

Age 50, male, paraanal abscess excision, massive bleeding when it is opened. On spraying the powder topically to the bleeding area, the black color is formed on contact because of the blood coagulation. The white color is the powder instantly not mixed up with the blood yet. Lastly, insert the long gauze into the anus.

EXAMPLE 11

Extraction of Teeth

Age 30, male, extraction of teeth, gum injected bleeds. Administering this powder topically to the bleeding area, the bleeding stops on contact and black blood coagulation forms at the same time. Wipe out the black coagulation in 10 seconds, stopped bleeding still persisted.

EXAMPLE 12

Extraction of Teeth for Chronic Hepatitis

Age 60, female, chronic hepatitis, has bleeding tendency, extraction of teeth causes massive bleeding. Upon applying this powder to the socket of the gum, the black coagulation forms on contact, and the bleeding in the socket stops on contact accordingly.

EXAMPLE 13

Finger Scratched

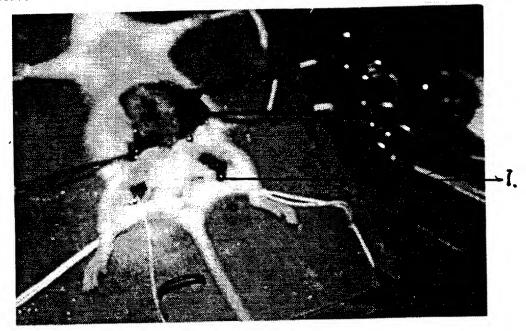
Myself, finger little scratched, slightly bleeds. Upon contact with the powder, the black color forms on contact.

EXAMPLE 14

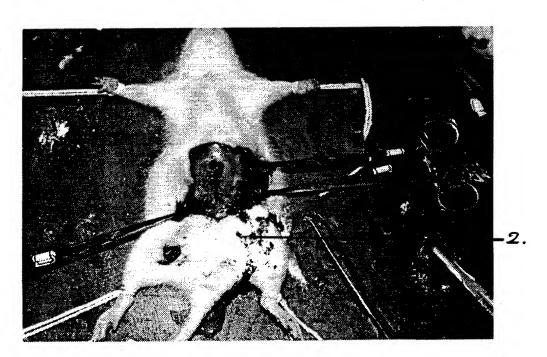
Normal, Liver Disease, Colon Cancer and Hemophilia Blood When tested in the tube, I milliliter of human blood requires 0.15 68 grams of powdered vitamin C to form black blood coagulation by shaking the tube with hand or stirrer machine. It takes 6 minutes to cause the black blood coagulation unmobile in the test tube for normal, liver diseases, colon cancer and hemophilia blood respectively. These experiments have evidenced that the mechanism of action of powdered vitamin C in the formation of black blood coagulation does not involve the coagulation factors.

I claim:

- 1. A therapeutic instant blood coagulant composition which comprises:
- (a) ascorbic acid, or L-threo-hex-2-enono-1,4-lactone, or vitamin C, and mixtures thereof;
 - (b) excipients.
- 2. The composition according to claim 1, wherein the ascorbic acid, or L-threo-hex-2-enono-1,4-lactone, or vitamin C, and excipients are in a powdered form.
- 3. The composition according to claim 1, wherein the ascorbic acid, or L-threo-hex-2-enono-1,4-lactone, or vitamin C, and excipients are in an aqueous form.
- 4. The composition according to claim 1, wherein the ascorbic acid, or L-threo-hex-2-enono-1,4-lactone, or vitamin C, and excipients are in a tablet form.
- 5. The composition according to claim 1, wherein sodium ascorbate is considered vitamin C.



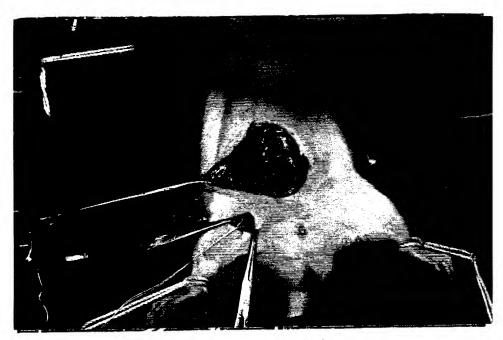
Photograph or Figure # 1



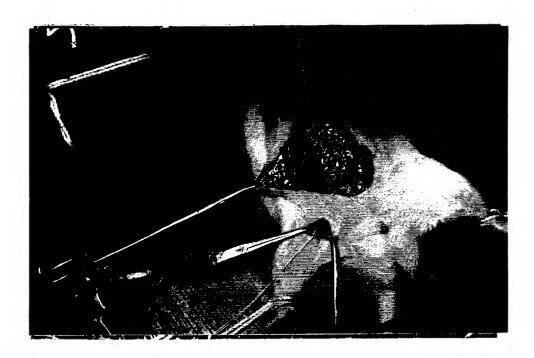
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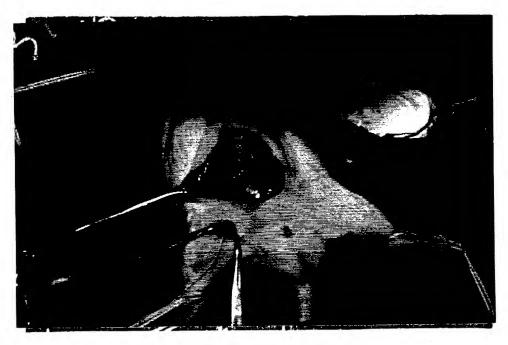
Photograph or Figure # 3



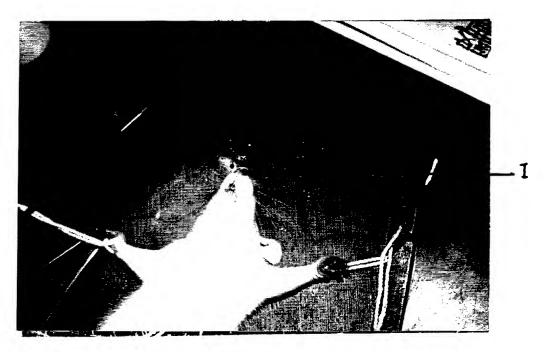
Photograph or Figure # 4



Photograph or Figure # 5_1



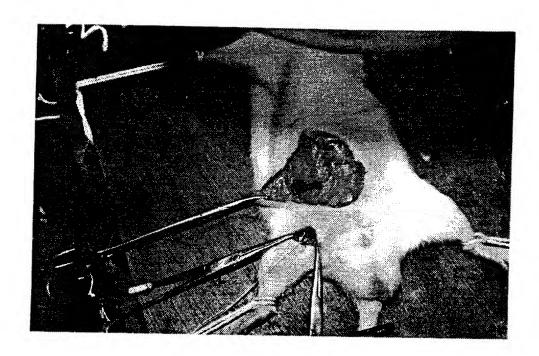
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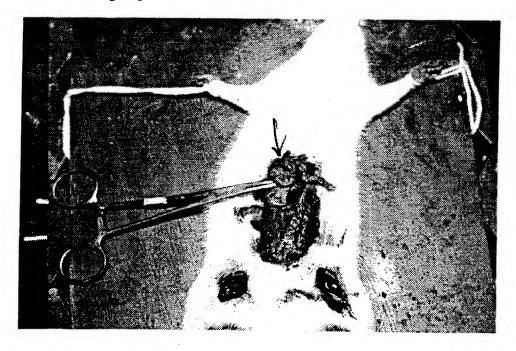
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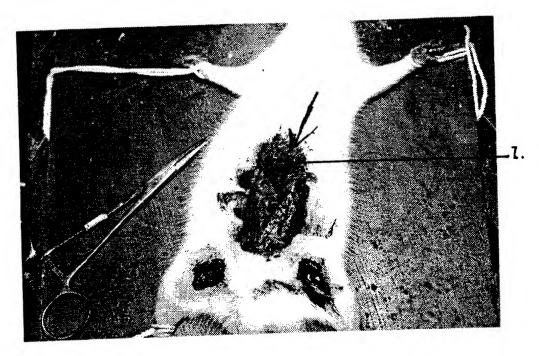


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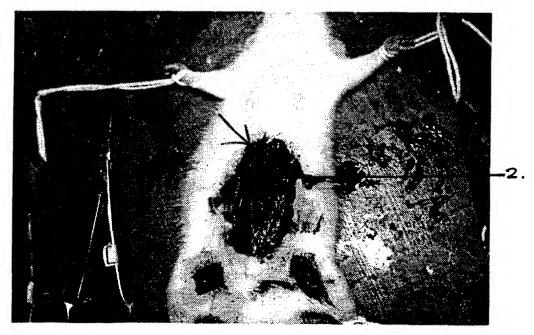
Photograph or Figure # 8



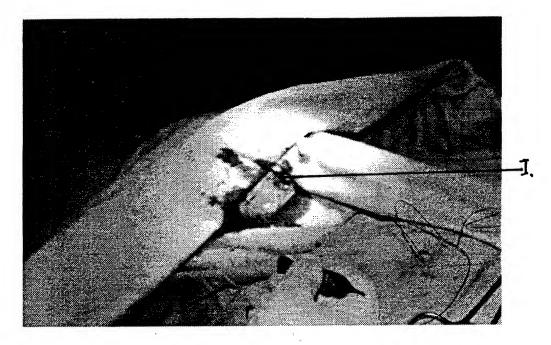


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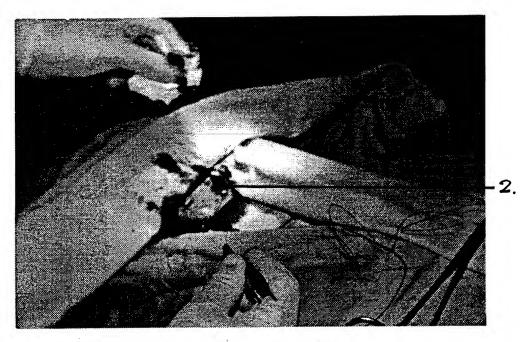
Photograph or Figure # 10



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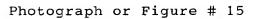
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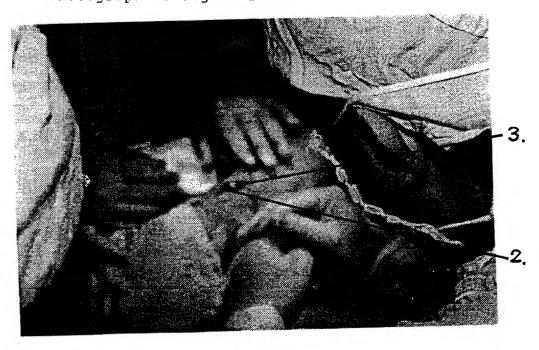


Photograph or Figure # 13



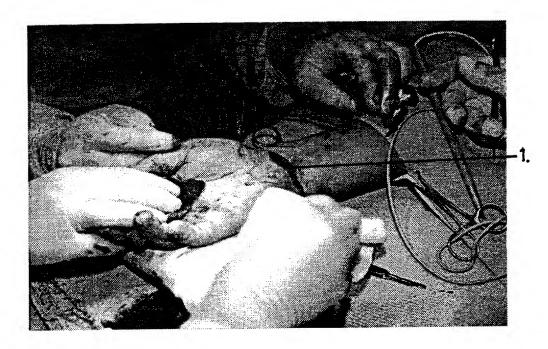
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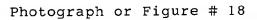


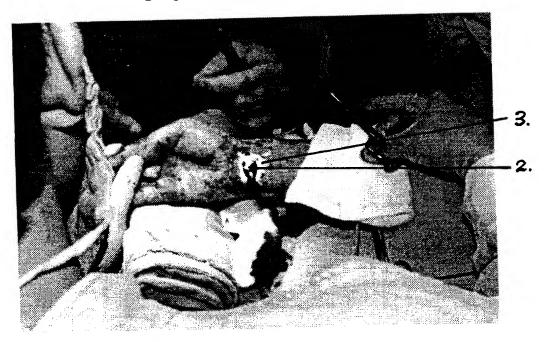


Photograph or Figure # 16



Photograph or Figure # 17







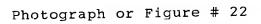
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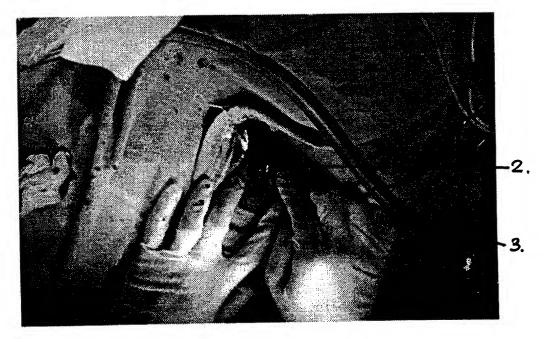


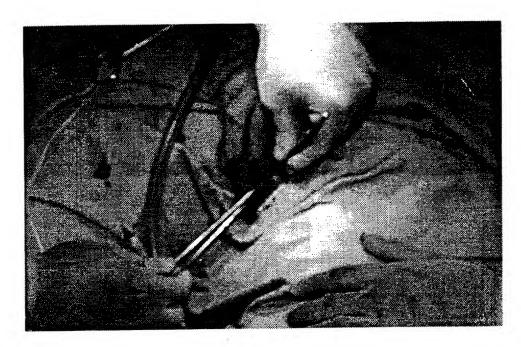
Photograph or Figure # 20



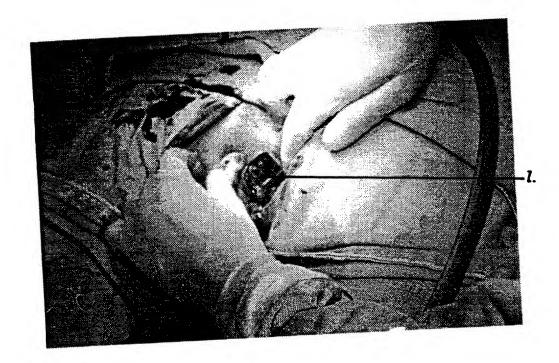
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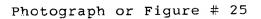


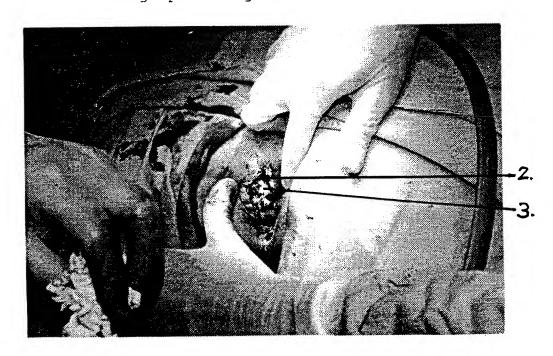


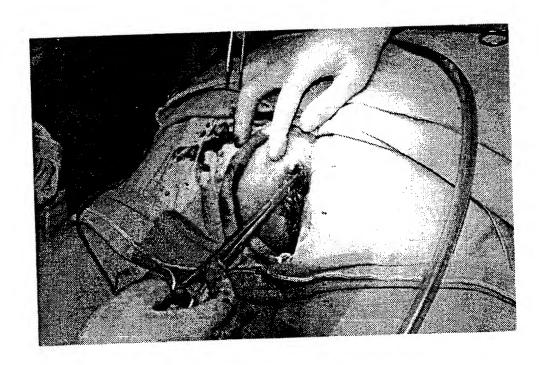
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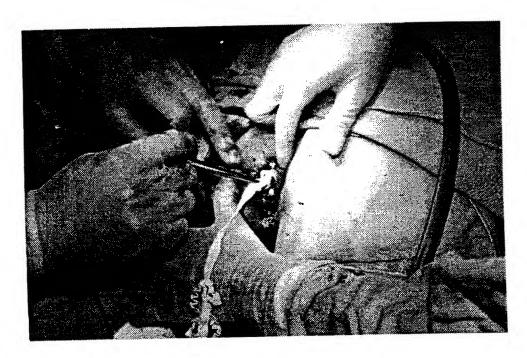
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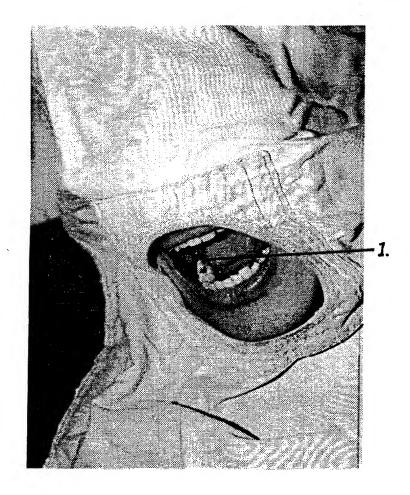




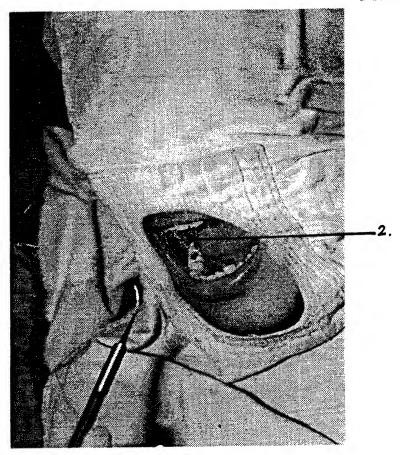


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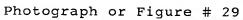


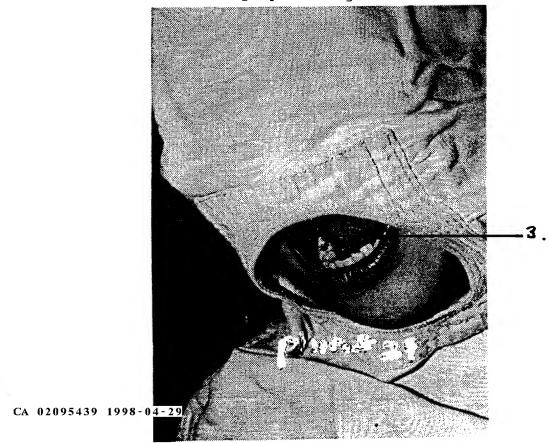


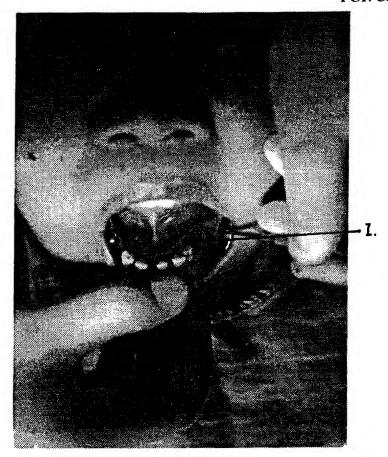
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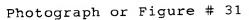
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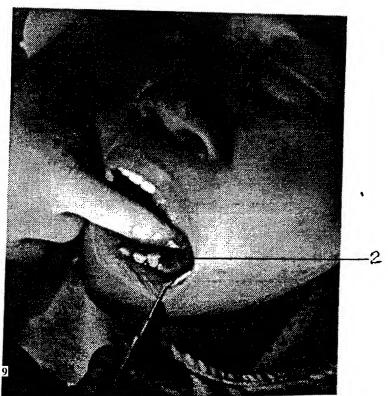


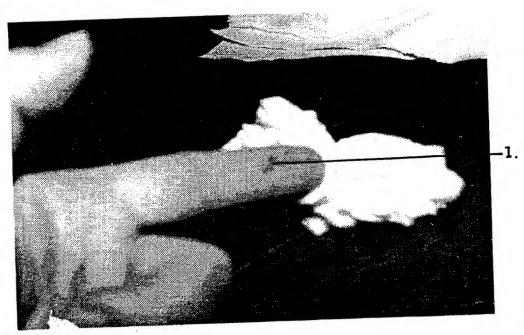




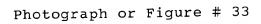
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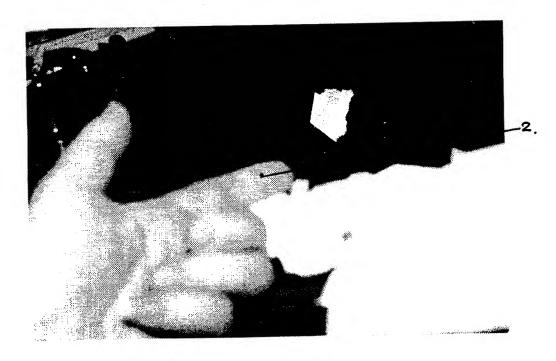




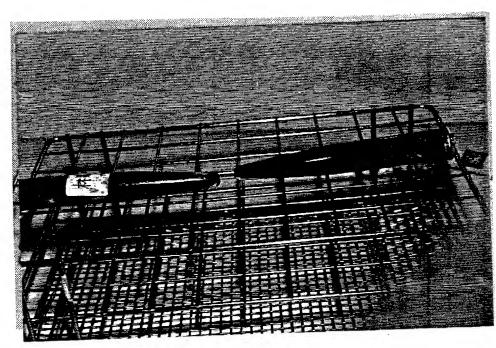


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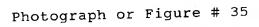


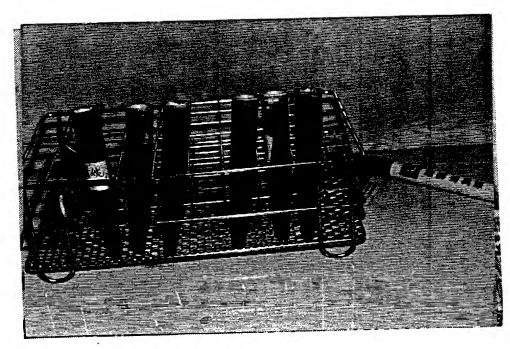


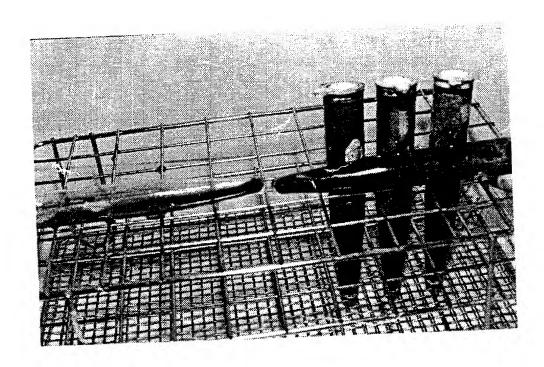




Photograph or Figure # 34







Photograph or Figure # 36

